

REMARKS**I. Claim Status**

Claims 3, 5-6, 8-11, 13, 17 and 18 are pending in this application.

In this Response, Claims 11, 13 and 18 are amended and claims 14-16 are cancelled.

II. Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 3, 5, 6, 8-10 and 13-18 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner refers to the variable R in claim 18, which is considered not to be in the list of substituents recited for the (C₁-C₆)alkyl group.

Applicants respectfully direct the Examiner's attention to the substituent NRC(=O)R⁴ in the second line of the substituents for group (b), which is an optionally substituted (C₁-C₆)alkyl group. As this substituent does contain a variable R, Applicants respectfully request that this rejection be withdrawn.

III. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 3, 5, 6, 8-11 and 13-18 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Specifically, it was alleged in the Office Action that even though the specification is enabling for making salts of the claimed compounds, it does not reasonably provide enablement for making hydrates and solvates of the claimed compounds.

Applicants submit that selection of a suitable solvent for a pharmaceutically acceptable solvate (hydrate if the solvent is water) of the claimed compounds is a routine matter for the skilled medicinal chemist. However, in order to progress the present application to allowance, claim 18 has been amended by deleting hydrates and solvates therefrom. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 13-16 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Specifically, it was alleged in the Office Action that even though the specification is enabling for the treatment of AIDS (or HIV infection), it does not reasonably provide enablement for the treatment of other diseases such as T-cell related disease, osteoporosis, chronic obstructive pulmonary disease (or COPD), asthma, cancer, leukemia, allergy, dermatoses, psoriasis and atopic dermatitis.

Applicants submit that the specification (especially pages 10-24) clearly describes the manner and process of both making and using the compounds of the present invention, and that the references previously provided to the Examiner, together with other literature cited in the application, provide sufficient guidance to one of skill in the art for a link between the PDE7 inhibitors of the present invention and the claimed diseases/disorders.

However, in order to progress the present application to allowance, claim 13 has been amended to define a method of treating AIDS (or HIV infection) by administration of a compound of the invention, and claims 14-16 have been cancelled. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Double Patenting

Claims 3, 5, 6, 8-11 and 13-18 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over final claims 1-6, 8-17 and 19 of recently allowed US Application No. 10/852,404 (Publication No. 2004/0214843 A1). Specifically, it is alleged that formula I of the present application overlaps with formula I of the allowed USSN 10/852,404 wherein (i) X_1 , X_2 , X_3 and X_4 are CR^1 ; (ii) R^1 is $Q1$; (iii) $Q1$ is hydrogen, halogen or OR^2 ; (iv) X is NR^9 (wherein R^9 is H); (v) Y is NR^{12} (wherein R^{12} is H); (vi) Z is O; and (vii) A is a 5-, 6- or 7-membered ring.

As will be demonstrated below, formula I of the present application does not overlap with formula I of the allowed US Application No. 10/852,404: the definition R^2 of the present formula I covers a number of substituents which are not covered by formula I of the allowed application. For the convenience of the Examiner, the groups of substituents (a) to (c) which together form the definition of R^2 will be discussed separately.

Group (a) – $R^2 = Q^1-Q^2-Q^3-Q^4$

Claim 1 of USSN 10/852,404	Claim 18 of the present application
X_1 may be X^5R^5	OR^2 must be present at 5-position
X^5 may be a single bond or lower alkylene optionally interrupted with i.a. O	Q^1 is a single bond or linear or branched (C_1-C_6)alkylene
R^5 may be cycloalkyl (defined as C_3-C_8 cycloalkyl: page 49 line 13) optionally interrupted (defined at page 49 lines 15 to 19) with i.a. N	Q^2 is a saturated 4 to 6-membered heterocycle comprising a nitrogen atom
Group may be substituted with heteroaryl, but only directly (not via an alkylene bridge); also definition of R^3+R^4+N implies connection via nitrogen atom	Q^3 (which must be present) is a linear (C_1-C_4)alkylene group; Q^4 is a 5 or 6-membered aromatic heterocycle comprising 1 to 4 N atoms, and which may optionally be substituted with methyl; Q^4 must also be bound to Q^3 via a carbon atom

Group (a) – $R^2 = Q^1-Q^2-Q^3-Q^4$ (alternative)

Claim 1 of USSN 10/852,404	Claim 18 of the present application
X_1 may be Q_1 ; Q_1 may be OR^2	OR^2 must be present at 5-position
R^2 may be Q_4 -cycloalkyl wherein Q_4 may be $(CH_2)_n$ ($n = 0$ to 4) and cycloalkyl is optionally interrupted with i.a. N	Q^1 is a single bond or linear or branched (C_1-C_6)alkylene; Q^2 is a saturated 4 to 6-membered heterocycle comprising a nitrogen atom
Group may be substituted with heteroaryl (NR^6R^7 wherein R^6+R^7+N may form a heterocyclic ring; heterocyclic includes heteroaryl: page 49 line 23), but only directly (not via an alkylene bridge); also definition of R^6+R^7+N implies connection via nitrogen atom	Q^3 (which must be present) is a linear (C_1-C_4)alkylene group; Q^4 is a 5 or 6-membered aromatic heterocycle comprising 1 to 4 N atoms, and which may optionally be substituted with methyl; Q^4 must also be bound to Q^3 via a carbon atom

The above tables show that there is no overlap between the definition of $Q^1-Q^2-Q^3-Q^4$ of the present application and that in the broadest disclosure and claims of allowed USSN 10/852,404. Therefore, the compound group (a) of the present application is distinct from allowed USSN 10/852,404.

Group (b) – R² = (C₁-C₆)alkyl (first substituent set)

Claim 1 of USSN 10/852,404	Claim 18 of the present application
X ₁ may be Q1; Q1 may be OR ²	OR ² must be present at 5-position
R ² may be lower alkyl (defined as C ₁ -C ₆ alkyl: page 48 lines 28-29) which may be further substituted with i.a. OR ⁶ , COOR ⁶ , NR ⁶ R ⁷ , NR ⁶ C(=O)R ⁷ , C(=O)NR ⁶ R ⁷ or SO ₂ NR ⁶ R ⁷	R ² is (C ₁ -C ₆)alkyl which is further substituted with OR ⁴ , COOR ⁴ , NR ⁴ R ⁵ , NRC(=O)R ⁴ , C(=O)NR ⁴ R ⁵ or SO ₂ NR ⁴ R ⁵
R ⁶ and R ⁷ may be hydrogen or lower alkyl which may be substituted with one or two groups selected from OR, COOR or NR ²³ R ²⁴ wherein R ²³ and R ²⁴ may be hydrogen or lower alkyl	R ⁴ and R ⁵ are (C ₁ -C ₆)alkyl which is further substituted (R ⁴) and may be further substituted (R ⁵) by 1 to 3 groups selected from S(=O)R ⁶ , SO ₂ R ⁶ , NR'C(=O)R ⁷ , NR'SO ₂ R ⁶ , C(=O)NR ⁷ R ⁸ , O-C(=O)NR ⁷ R ⁸ , SO ₂ NR ⁷ R ⁸

The above table shows that the substituents which must be present on the lower alkyl groups R⁴ (and optionally on R⁵) of the present application do not overlap with the substituents which may be present on the equivalent alkyl groups in allowed USSN 10/852,404: the substituent groups OR, COOR or NRR⁸ are not included in the list of possible substituents for the groups R⁴ and R⁵ of the present application. Additionally, as a substituent must be present on the alkyl group R⁴ in the present application, the possibility in the present application of R⁴ being unsubstituted alkyl is excluded. The compound group (b) of the present application is therefore distinct from allowed USSN 10/852,404.

Group (c) – R² = (C₁-C₆)alkyl (second substituent set)

Claim 1 of USSN 10/852,404	Claim 18 of the present application
X ₁ may be Q1; Q1 may be OR ²	OR ² must be present at 5-position
R ² may be lower alkyl (defined as C ₁ -C ₆ alkyl: page 48 lines 28-29) which may be further substituted with lower alkyl, halogen, CN, CH ₃ , SO ₃ H, SO ₂ CH ₃ , C(=O)-NH-SO ₂ -CH ₃ , CF ₃ , OR ⁶ , COOR ⁶ , C(=O)R ⁶ , NR ⁶ R ⁷ , NR ⁶ C(=O)R ⁷ , C(=O)NR ⁶ R ⁷ or SO ₂ NR ⁶ R ⁷	R ² is (C ₁ -C ₆)alkyl which is substituted with 1 to 3 groups selected from OC(=O)R ^{4a} , SR ^{4a} , S(=O)R ³ , NR ^a COOR ^{4a} , NR ^a -C(=O)-NR ^{4a} NR ^{5a} , NR ^a -SO ₂ -NR ^{4a} R ^{5a} , NR ^a -SO ₂ -R ³

As the above table shows, none of the substituents in the second substituent list for the alkyl group R^2 in the present application are present in the list of substituents for the equivalent alkyl group R^2 in allowed USSN 10/852,404. Additionally, as a substituent must be present on the alkyl group R^2 in the present application, the possibility in the present application of R^2 being unsubstituted alkyl is excluded. The compound group (c) of the present application is therefore distinct from allowed USSN 10/852,404.

Furthermore, contrary to what is alleged in the Office Action, the table below demonstrates that no specific compounds of allowed USSN 10/852,404 fall within each group of claim 1 of the present application.

USSN 10/852,404 Ex no	Outside group (a) because...	Outside group (b) because...	Outside group (c) because...
67	No further substituent group Q^3 - Q^4 present	N , R^4 and R^5 may not form a ring	Not substituted with any of required groups
68	No heterocycle substituting alkoxy group	Alkyl group R^4 not substituted	Not substituted with any of required groups
69	No heterocycle substituting alkoxy group	R^4 and R^5 may not both be H	Not substituted with any of required groups
70	No heterocycle substituting alkoxy group	Alkyl group R^4 not substituted	Not substituted with any of required groups
71	No heterocycle substituting alkoxy group	Substituents on alkyl group R^4 don't include NH_2	Not substituted with any of required groups
72	No heterocycle substituting alkoxy group	Alkyl group R^4 not substituted	Not substituted with any of required groups
73	No heterocycle substituting alkoxy group	Alkyl group R^4 not substituted	Not substituted with any of required groups
74	No heterocycle substituting alkoxy group	R^4 cannot be H	Not substituted with any of required groups
75	No heterocycle substituting alkoxy group	R^4 cannot be H	Not substituted with any of required groups
76	No heterocycle substituting alkoxy group	Substituents on alkyl group R^4 don't include SO_3H	Not substituted with any of required groups
77	Heterocycle doesn't include N atom; Q^1 can't include O atom	Substituents on alkyl group R^4 don't include heterocycle	Not substituted with any of required groups

78	No heterocycle substituting alkoxy group	R ⁴ cannot be H	Not substituted with any of required groups
79	Heterocycle is aromatic and doesn't include N atom	Substituents on alkyl group R ⁴ don't include heteroaryl	Not substituted with any of required groups
80	Heterocycle is aromatic and doesn't include N atom	Substituents on alkyl group R ⁴ don't include heteroaryl	Not substituted with any of required groups
81	No heterocycle substituting alkoxy group	Substituents on alkyl group R ⁴ don't include CN	Not substituted with any of required groups
82	Heterocycle is aromatic	Substituents on alkyl group R ⁴ don't include heteroaryl	Not substituted with any of required groups
83	Heterocycle is aromatic	Substituents on alkyl group R ⁴ don't include heteroaryl	Not substituted with any of required groups
92	Present application only allows H in 6-position		
93	Present application only allows all-carbon spirocycle (may not include O atom)		
96	No heterocycle substituting alkoxy group	Alkyl group R ⁴ on N atom not substituted; R ⁴ cannot be H when part of OR ⁴	Not substituted with any of required groups
97	No heterocycle substituting alkoxy group	Alkyl group R ⁴ on N atom not substituted; R ⁴ cannot be H when part of OR ⁴	Not substituted with any of required groups
98	No heterocycle substituting alkoxy group	Substituents on alkyl group R ⁴ don't include CO ₂ Et	Not substituted with any of required groups
99	No heterocycle substituting alkoxy group	Substituents on alkyl group R ⁴ don't include CO ₂ H	Not substituted with any of required groups

The above demonstrates that the claims of the present application do not overlap with USSN 10/852,404. Furthermore, there is nothing in USSN 10/852,404 which would motivate the skilled person to consider modifying the compounds disclosed therein to arrive at the compounds of the present invention. We respectfully request that this objection be withdrawn.

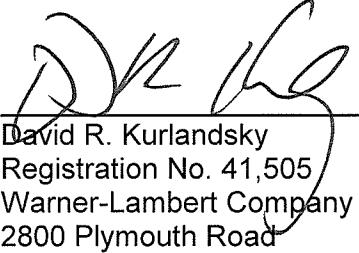
VI. Conclusion

In view of the amendments and remarks made above, Applicants believe that this application is now in condition for allowance. Reconsideration and allowance of Claims 3, 5-6, 8-11, 13, 17 and 18 is respectfully requested.

The Commissioner is authorized to charge any fee or credit any over payment in connection with this communication to our Deposit Account No. 23-0455.

Respectfully submitted,

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